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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,387	12/12/2003	Marie-Madeleine Cals-Grierson	016800-655	8526

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EXAMINER	
HENLEY III, RAYMOND J	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,387	CALS-GRIERSON, MARIE-MADELEINE	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *2-5,7-14,16,17 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,15,18-20,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-25 ARE PRESENTED FOR EXAMINATION

Applicant's "Reply and Amendment In Response To Election/Restriction Requirement", Information Disclosure Statement, Foreign Priority document and an English language translation of PCT/FR02/02064, filed June 14, 2002, (of which the present application is a continuation), have been received and entered into the application.

Accordingly, the specification at page 1, paragraph [0002], and claims 2-17, 20 and 21 have been amended and claims 24 and 25 have been added. Also, as reflected by the attached, completed copy of "Substitute for form 1449A/PTO & 1449B/PTO", (1 sheet), the Examiner has considered the cited references. Additionally, acknowledgement is made of Applicant's claim for foreign priority based on the French Patent Document No. 01 07878, filed June 15, 2001.

Because Applicant has submitted an English language translation of PCT/FR02/02064, the effective date of the present application, for the purposes of examination and in the absence of an English language translation of the French Patent Document, is that of the PCT document, i.e., June 14, 2002, (see 37 CFR § 1.55 and MPEP § 201.15).

Election/Restrictions

Applicant's election with traverse of Group IX in the above referenced reply at pages 11-12 is acknowledged. The traversal is on the grounds that it would not be unduly burdensome for Examiner to consider all of Applicant's claims because such claims require the use of only a single compound, i.e., N,N'-bis(2-pyridyl)methyl-N,N'-bis(3,4,5-trimethoxybenzyl)-ethylenediamine. Also, Applicant points out that the methods, as claimed, are all reflections of the capability of that compound to inhibit NO-synthase.

This traversal is not found persuasive because of the number and nature of therapeutic objectives covered by each of the grouped inventions. The Examiner maintains that each of the inventions of the present application are patentably distinct and independent based upon the fact that each invention is directed to distinctly different subject matter from any one or more of the other inventions and that each invention is capable of supporting separate patents.

Notwithstanding that Applicant may have elucidated a mechanism of action that is common to all such objectives, i.e., the compound's ability to inhibit NO-synthase, it remains that each of the claimed therapeutic objectives may involve different etiologies, pathophysiological manifestations and art-recognized therapies. The performance of a complete and comprehensive search of any one of the inventions would not necessarily result in a complete search of the prior art for any other invention based on the evidence of distinctly different ultimate function or effect. Execution of a search encompassing all of Applicant's inventions, when taken together with the Examiner's requisite consideration of the findings of such a search in accordance with the requirements of the law under 35 U.S.C. §§ 101, 102, 103 and 112, compels the Examiner to maintain that an undue burden would be met if all of the inventions of the present application were to be considered together.

Upon a cursory review of the pertinent art, and in effort to consider as much subject matter as is reasonable, the Examiner will modify the restriction requirement to the extent that the examined subject matter will include not only that of elected, (with traverse), Group IX, claim 15, but also of Group III, claim 6, directed to a regime or regimen for inhibiting NO-synthase and thus treating intrinsic and/or extrinsic aging. Additionally claim 20, which was erroneously placed into group XII by the Examiner, (as pointed out by Applicant at page 10 of the response

and for which the Examiner regrets), will be examined. Claim 20 is directed to a cosmetic regime or regimen for treating a disorder associated with NO-synthesis, comprising topically applying the claimed compound onto the skin, the hair and/or mucous membranes of an individual in need thereof.

The requirement is otherwise still deemed proper and is therefore made **FINAL**.

Claims 2-5, 7-14, 16, 17 and 21-23 are withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claims 1, 6, 15, 18-20, 24 and 25 are herein acted on the merits.

References Cited by the Examiner

The reference cited on the attached form PTO-892 and not relied on by the Examiner, i.e., Pauly et al., (U.S. 6,511,684 B1), is included to show the general state of the art concerning cosmetic/pharmaceutical compositions for the control of aging skin and hyper-pigmentation, i.e., hypermelanosis, conditions.

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. § 102, a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genetech, Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue,* 766 F2d531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). To anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365, 52

U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber,* 128 F.3d 1473, 1477, 44 U.S.P.Q. 1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.,* 190 F.3d 1342, 1347, 51 U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). To inherently anticipate, the prior art must necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile*, 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery of the mechanism underlying a known process does not make it patentable. See also MPEP §§ 2112, 2112.02 and 2145(II).

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6 and 18-20 rejected under 35 U.S.C. 102(b) as being anticipated by Galey et al., (U.S. Patent No. 5,760,037; cited by Applicant) who teach that the application of a pharmaceutical, (a.k.a. therapeutic)/cosmetic composition comprising, *inter alia*, 0.50% of N,N'-bis(2-pyridyl)methyl-N,N'-bis(3,4,5-trimethoxybenzyl)-ethylenediamine as the active agent "applied regularly once per day, preferably in the evening, this composition makes it possible to prevent skin aging in an especially significant way.". The patentees further instruct that such a composition may contain a proportion of active agent of from 0.001 to 10% by weight of the entire composition.

The patentees do not teach the full or exact range of proportions as in present claims 18 or 19, but clearly teach proportions which overlap and touch the ranges presently claimed. Also, as evidenced by the dependent nature of claims 18 and 19, the expressly claimed proportion ranges therein, i.e., 0.0001 to 20%, (claim 18) and 0.005 to 10%, (claim 19), underlying the functional recitations in the claims for "a thus effective amount" (claim 1) and "a thus effective NO-synthase inhibiting amount" (claims 6 and 20) and thus are also anticipated by the reference.

The requirement in claim 6 for "intrinsic and/or extrinsic aging" is met by the reference teaching of aging in general because the genus "aging" is sufficiently small as to have placed in the possession of the public the presently claimed two species. See MPEP 2144.08(II)(A)(4)(a), under the ultimate sub-heading "Consider the Size of the Genus".

Also, the requirements in claims 1, "a regime or regimen for inhibiting NO-synthase", and in claim 20, i.e., "treating a disorder associated with NO-synthesis" are inherently met by the teaching of treating aging in the reference. The fact that the reference does not highlight the compound's effect on NO in the system does not distinguish the presently claimed subject matter from that of the reference because in both the present claims and the reference, the same compound is administered to the same host and would be present in the same environment. It therefore must necessarily be so that the compound functions in the prior art in the same manner as in the present claims.

Once the compound has entered the system of the patient, neither Applicant nor the patentees have any control of the function of the compound. This is because the function of the compound and the compound itself are inseparable. Also, see MPEP §§ 2112, 2112.02, which is herein incorporated by reference.

Accordingly, for the above reasons, the claims are deemed properly rejected.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 15, 18-20, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galey et al., for the reasons above, which are herein incorporated by reference, in view of Schlitt (U.S. Patent No. 4,959,551; cited by the Examiner) and Browning (U.S. Patent No. 6,828,460; cited by the Examiner).

The differences between the above and the claimed subject matter lies in that Galey et al. fail to highlight:

(1) "inhibiting NO-synthase and thus inhibiting melanogenesis induced UV-A and/or UV-B radiation and/or treating a hypermelanosis disorder' (claim 15); and

(2) the full range of proportion expressly recited in present claim 18 (and also present claim 24) and encompassed by the above referenced functional language in claims 1, 6, 15 and 20.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(1) Galey et al. teaches that the compound may be used to protect an organism against oxidizing stress (col. 1, lines 10-13) and that exposure to ultra-violet rays, (a.k.a., radiation), promotes such stress (col. 1, lines 21-26). One of ordinary skill in the art would have appreciated that exposure to ultra-violet rays would lead to melanogenesis induced by UV-A and/or UV-B radiation and thus that the treatment of Galey et al. would afford inhibition of melanogenesis caused thereby because it was known in the art that UV-A and UV-B radiation caused melanogensis, while Galey et al. teach that the claimed compound is effective for offering protection against ultraviolet rays. The term "ultraviolet rays" is a genus that is so small so as to have had the artisan once envisage each sub-type of radiation therein, including type A and B.

In support of the above position, the Examiner relies on Schlitt who teaches that both UV-A and UV-B are ultraviolet wavelengths which affect the skin by stimulating melanocytes to produce melanin, (col. 1, lines 13-35, especially lines 22-35). Further supporting the conclusion that the compounds of Galey et al. and the present claims would afford protection against the effects of such radiation is the further teaching of Galey et al. that the compound is an antioxidant compound (col. 4, line 44), while Schlitt teaches that antioxidants not only inhibit oxidation of pigment, i.e., oxidation of melanin which causes it to become darker (Schlitt at col. 1, lines 43-56, "In order to render the pigmentation process effective, the melanin granules must darken (oxidize). This requires a higher dosage of longer wave UVA" and "These antioxidants not only inhibit oxidation of pigment, but can reverse the process").

It would have been further obvious to do what is in present claim 15, such as treating a hypermelanosis disorder, because Browning et al. teaches the treatment of several such disorders, e.g., idiopathic melasma (col. 2, lines 21-34), which a depigmenting composition which

may include an antioxidant compound (col. 38, line 60 and col. 39, line 63), while, as noted above, it was known that the claim designated compound was an antioxidant (Galey et al. at col. 4, line 44). The artisan would have been motivated to include the compounds of Galey et al. in the composition and method of Browning et al. based on the express teachings relied on above which would have been seen as advantageous to the artisan.

It is noted that the above reasoning does not include the inhibition of NO-synthase as set forth in the present claims. The reasoning is nevertheless proper because it is not required that the prior art reason and Applicant's be the same for accomplishing the same, ultimate therapeutic effect. See MPEP § 2144 under the heading "Rationale Different From Applicant's Is Permissible" where it is set forth that "The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972)".

(2) At col. 4, line 36, Galey et al. indicate that their express proportioning is exemplary, i.e., "the active compound corresponding to formula (I) is *normally* present in a proportion of 0.001 to 10% by weight of the total weight of the composition.". Such would have indicated to one of ordinary skill in the art that the proportioning of ingredients should be varied to account for the less than normal circumstances that would be met. "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105

USPQ 233, 235 (CCPA 1955)" (see MPEP 2144.05(II)). The determination of the optimum dosage regimen to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art and such determination would have been made on a case-by-case basis depending on the severity of the condition being treated.

Accordingly, for the above reasons, the claims are deemed properly rejected.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

March 11, 2006